Amendments to the Specification:

Please replace the paragraph beginning at page 33, line 19, with the following redlined paragraph:

T cells may be stimulated with WT1 polypeptide, polynucleotide encoding a WT1 polypeptide and/or an antigen presenting cell (APC) that expresses a WT1 polypeptide. Such stimulation is performed under conditions and for a time sufficient to permit the generation of T cells that are specific for the WT1 polypeptide. Preferably, a WT1 polypeptide or polynucleotide is present within a delivery vehicle, such as a microsphere, to facilitate the generation of antigen-specific T cells. Briefly, T cells, which may be isolated from a patient or a related or unrelated donor by routine techniques (such as by ~~Ficoll~~FICOLL®/~~Hypaque~~ HYPAQUE® density gradient centrifugation of peripheral blood lymphocytes), are incubated with WT1 polypeptide. For example, T cells may be incubated *in vitro* for 2-9 days (typically 4 days) at 37°C with WT1 polypeptide (*e.g.,* 5 to 25 μg/ml) or cells synthesizing a comparable amount of WT1 polypeptide. It may be desirable to incubate a separate aliquot of a T cell sample in the absence of WT1 polypeptide to serve as a control.

Please replace the paragraph beginning at page 42, line 21, with the following redlined paragraph:

Any of a variety of non-specific immune response enhancers, such as adjuvants, may be employed in the vaccines of this invention. Most adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a stimulator of immune responses, such as lipid A, *Bortadella pertussis* or *Mycobacterium tuberculosis* derived proteins. Suitable non-specific immune response enhancers include alum-based adjuvants (*e.g.*, ~~Alhydrogel~~ ALLHYDROGEL®, ~~Rehydragel~~ REHYDRAGEL®, aluminum phosphate, Algammulin, aluminum hydroxide); oil based adjuvants (Freund's adjuvant (FA), Specol, RIBI, ~~TiterMax~~ TITERMAX®, ~~Montanide~~ MONTANIDE® ISA50 or ~~Montanide~~ MONTANIDE® ISA 720 (Seppic, France); cytokines (*e.g.,* GM-CSF or ~~Flat3~~FLT3-ligand); microspheres; nonionic block copolymer-based adjuvants; dimethyl dioctadecyl

ammoniumbromide (DDA) based adjuvants AS-1, AS-2 (Smith Kline Beecham); Ribi Adjuvant system based adjuvants; QS21 (Aquila); saponin based adjuvants (crude saponin, the saponin Quil A); muramyl dipeptide (MDP) based adjuvants such as SAF (Syntex adjuvant in its microfluidized form (SAF-m)); dimethyl-dioctadecyl ammonium bromide (DDA); human complement based adjuvants *m. vaccae* and derivatives; immune stimulating complex (iscom) based adjuvants; inactivated toxins; and attenuated infectious agents (such as *M. tuberculosis*).

Please replace the paragraph beginning at page 43, line 8, with the following redlined paragraph:

Additional illustrative adjuvants for use in the pharmaceutical compositions of the invention include ~~Montanide~~ MONTANIDE® ISA 720 (Seppic, France), SAF™ (Chiron, California, United States), ISCOM®~~S~~ s (CSL), MF-59™ (Chiron), the SBAS™, series of adjuvants (*e.g.,* SBAS™-2 or SBAS™-4, available from SmithKline Beecham, Rixensart, Belgium), Detox (~~Enhanzyn~~ENHANZYN®) (Corixa, Hamilton, MT), RC-529™ (Corixa, Hamilton, MT) and other aminoalkyl glucosaminide 4-phosphates (AGPs), such as those described in pending U.S. Patent Application Serial Nos. 08/853,826 (U.S. Patent No. 6,113,918) and 09/074,720 (U.S. Patent No. 6,355,257), the disclosures of which are incorporated herein by reference in their entireties, and polyoxyethylene ether adjuvants such as those described in WO 99/52549A1.

Please replace the paragraph beginning at page 44, line 7, with the following redlined paragraph:

As noted above, within certain embodiments, immune response enhancers are chosen for their ability to preferentially elicit or enhance a T cell response (*e.g.,* $CD4^+$ and/or $CD8^+$) to a WT1 polypeptide. Such immune response enhancers are well known in the art, and include (but are not limited to) ~~Montanide~~ MONTANIDE® ISA50, Seppic MONTANIDE® ISA 720, cytokines (*e.g.,* GM-CSF, Flat3-ligand), microspheres, dimethyl dioctadecyl ammoniumbromide (DDA) based adjuvants, AS-1 (Smith Kline Beecham), AS-2 (Smith Kline Beecham), Ribi Adjuvant system based adjuvants, QS21 (Aquila), saponin based adjuvants

(crude saponin, the saponin Quil A), Syntex adjuvant in its microfluidized form (SAF-m), MV, ddMV (Genesis), immune stimulating complex (iscom) based adjuvants and inactivated toxins.

Please replace the paragraph beginning at page 44, line 17, with the following redlined paragraph:

In another aspect of the present invention, compositions may comprise adjuvants for eliciting a predominantly Th1-type response. Certain preferred adjuvants for eliciting a predominantly Th1-type response include, for example, a combination of monophosphoryl lipid A (MPL®), preferably 3-de-O-acylated monophosphoryl lipid A (3D-MPL™), together with an aluminum salt. MPL® adjuvants, such as MPL-SE, are available from Corixa Corporation (Seattle, WA; *see*, for example, US Patent Nos. 4,436,727; 4,877,611; 4,866,034 and 4,912,094, incorporated herein in their entirety). CpG-containing oligonucleotides (in which the CpG dinucleotide is unmethylated) also induce a predominantly Th1 response. Such oligonucleotides are well known and are described, for example, in WO 96/02555, WO 99/33488 and U.S. Patent Nos. 6,008,200 and 5,856,462. Immunostimulatory DNA sequences are also described, for example, by Sato et al., *Science 273*:352, 1996. Another preferred adjuvant comprises a saponin, such as Quil A, or derivatives thereof, including QS21 and QS7 (Aquila Biopharmaceuticals Inc., Framingham, MA); Escin; Digitonin; or *Gypsophila* or *Chenopodium quinoa* saponins . Other preferred formulations include more than one saponin in the adjuvant combinations of the present invention, for example combinations of at least two of the following group comprising QS21, QS7, Quil A, β-escin, or digitonin.

Please replace the paragraph beginning at page 53, line 25, with the following redlined paragraph:

Following immobilization, the remaining protein binding sites on the support are typically blocked. Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin, ~~Tween~~ TWEEN® 20™ (Sigma Chemical Co., St. Louis, MO), heat-inactivated normal goat serum (NGS), or BLOTTO (buffered solution of nonfat dry milk which also contains a preservative, salts, and an antifoaming agent). The support is then incubated with

a biological sample suspected of containing specific antibody. The sample can be applied neat, or, more often, it can be diluted, usually in a buffered solution which contains a small amount (0.1%-5.0% by weight) of protein, such as BSA, NGS, or BLOTTO. In general, an appropriate contact time (*i.e.*, incubation time) is a period of time that is sufficient to detect the presence of antibody that specifically binds WT1 within a sample containing such an antibody. Preferably, the contact time is sufficient to achieve a level of binding that is at least about 95% of that achieved at equilibrium between bound and unbound antibody. Those of ordinary skill in the art will recognize that the time necessary to achieve equilibrium may be readily determined by assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

Please replace the paragraph beginning at page 54, line 12, with the following redlined paragraph:

Unbound sample may then be removed by washing the solid support with an appropriate buffer, such as PBS containing 0.1% ~~Tween~~ TWEEN® 20™. A detection reagent that binds to the immunocomplexes and that comprises a reporter group may then be added. The detection reagent is incubated with the immunocomplex for an amount of time sufficient to detect the bound antibody. An appropriate amount of time may generally be determined by assaying the level of binding that occurs over a period of time. Unbound detection reagent is then removed and bound detection reagent is detected using the reporter group. The method employed for detecting the reporter group depends upon the nature of the reporter group. For radioactive groups, scintillation counting or autoradiographic methods are generally appropriate. Spectroscopic methods may be used to detect dyes, luminescent groups and fluorescent groups. Biotin may be detected using avidin, coupled to a different reporter group (commonly a radioactive or fluorescent group or an enzyme). Enzyme reporter groups (*e.g.,* horseradish peroxidase, beta-galactosidase, alkaline phosphatase and glucose oxidase) may generally be detected by the addition of substrate (generally for a specific period of time), followed by spectroscopic or other analysis of the reaction products. Regardless of the specific method employed, a level of bound detection reagent that is at least two fold greater than background

(*i.e.,* the level observed for a biological sample obtained from a disease-free individual) indicates the presence of a malignant disease associated with WT1 expression.

Please replace the paragraph beginning at page 58, line 3, with the following redlined paragraph:

Sera from adult patients with *de nova* AML or CML were studied for the presence of WT1 specific Ab. Recombinant proteins were adsorbed to TC microwell plates (Nunc, Roskilde, Denmark). Plates were washed with PBS/0.5% ~~Tween~~ TWEEN® 20 and blocked with 1% BSA/PBS/0.1% ~~Tween~~ TWEEN® 20. After washing, serum dilutions were added and incubated overnight at 4°C. Plates were washed and Donkey anti-human IgG-HRP secondary antibody was added (Jackson-Immunochem, West Grove, PA) and incubated for 2h at room temperature. Plates were washed, incubated with TMB Peroxidase substrate solution (Kirkegaard and Perry Laboratories, MA), quenched with 1N H_2SO_4, and immediately read (Cyto-Fluor 2350; Millipore, Bedford, MA).

Please replace the paragraph beginning at page 60, line 1, with the following redlined paragraph:

Detection of existent antibodies to WT1 in patients with leukemia strongly implied that it is possible to immunize to WT1 protein to elicit immunity to WT1. To test whether immunity to WT1 can be generated by vaccination, mice were injected with TRAMP-C, a WT1 positive tumor cell line of B6 origin. Briefly, male B6 mice were immunized with 5 x 10^6 TRAMP-C cells subcutaneously and boosted twice with 5 x 10^6 cells at three week intervals. Three weeks after the final immunization, sera were obtained and single cell suspensions of spleens were prepared in RPMI 1640 medium (GIBCO®) with 25μM β-2-mercaptoethanol, 200 units of penicillin per ml, 10mM L-glutamine, and 10% fetal bovine serum.

Please replace the paragraph beginning at page 61, line 9, with the following redlined paragraph:

B6 mice were immunized with a group of WT1 peptides or with a control peptide. Peptides were dissolved in 1ml sterile water for injection, and B6 mice were immunized 3 times at time intervals of three weeks. Adjuvants used were CFA/IFA, GM-CSF, and ~~Montinide~~MONTANIDE®. The presence of antibodies specific for WT1 was then determined as

described in Examples 1 and 2, and proliferative T cell responses were evaluated using a standard thymidine incorporation assay, in which cells were cultured in the presence of antigen and proliferation was evaluated by measuring incorporated radioactivity (Chen et al., *Cancer Res. 54*:1065-1070, 1994). In particular, lymphocytes were cultured in 96-well plates at $2x10^5$ cells per well with $4x10^5$ irradiated (3000 rads) syngeneic spleen cells and the designated peptide.

Please replace the paragraph beginning at page 97, line 2, with the following redlined paragraph:

Peptide binding to C57Bl/6 murine MHC was confirmed using the leukemia cell line RMA-S, as described by Ljunggren et al., *Nature 346*:476-480, 1990. In brief, RMA-S cells were cultured for 7 hours at 26°C in complete medium supplemented with 1% FCS. A total of 10^6 RMA-S cells were added into each well of a 24-well plate and incubated either alone or with the designated peptide (25ug/ml) for 16 hours at 26°C and additional 3 hours at 37°C in complete medium. Cells were then washed three times and stained with fluorescein isothiocyanate-conjugated anti D^b or anti-K^b antibody (PharMingen, San Diego, CA). Labeled cells were washed twice, resuspended and fixed in 500ul of PBS with 1% paraformaldehyde and analyzed for fluorescence intensity in a flow cytometer (Becton-Dickinson ~~FACSCalibur~~FACSCALIBUR®™). The percentage of increase of D^b or K^b molecules on the surface of the RMA-S cells was measured by increased mean fluorescent intensity of cells incubated with peptide compared with that of cells incubated in medium alone.

Please replace the paragraph beginning at page 101, line 6, with the following redlined paragraph:

Mononuclear cells were isolated by density gradient centrifugation, and were immediately frozen and stored at -80°C until analyzed by RT-PCR for the presence of WT1 specific mRNA. RT-PCR was generally performed as described by Fraizer et al., *Blood 86*:4704-4706, 1995. Total RNA was extracted from 10^7 cells according to standard procedures. RNA pellets were resuspended in 25 µL diethylpyrocarbonate treated water and used directly for reverse transcription. The zinc-finger region (exons 7 to 10) was amplified by PCR as a 330 bp

mouse cDNA. Amplification was performed in a thermocycler during one or, when necessary, two sequential rounds of PCR. ~~AmpliTaq~~ AMPLITAQ® DNA Polymerase (Perkin Elmer Cetus, Norwalk, CT), 2.5 mM $MgCl_2$ and 20 pmol of each primer in a total reaction volume of 50µl were used. Twenty µL aliquots of the PCR products were electrophoresed on 2% agarose gels stained with ethidium bromide. The gels were photographed with ~~Polaroid~~ POLAROID® film (Polaroid 667, Polaroid Ltd., Hertfordshire, England). Precautions against cross contamination were taken following the recommendations of Kwok and Higuchi, *Nature 339*:237-238, 1989. Negative controls included the cDNA- and PCR-reagent mixes with water instead of cDNA in each experiment. To avoid false negatives, the presence of intact RNA and adequate cDNA generation was evaluated for each sample by a control PCR using β-actin primers. Samples that did not amplify with these primers were excluded from analysis.

Please replace the paragraph beginning at page 107, line 20, with the following redlined paragraph:

The PCR products were digested with EcoRI and cloned into pPDM His (a modified pET28 vector with a His tag in frame on the 5′ end) which has been digested with Eco72I and EcoRI. The constructs were confirmed to be correct through sequence analysis and transformed into BL21 pLys S and ~~BL21~~ BL21-~~CodonPlus~~ CODONPLUS® cells or BLR pLys S and BL21-CODONPLUS® ~~BLR CodonPlus~~ cells.

Please replace the paragraph beginning at page 108, line 18, with the following redlined paragraph:

The PCR product was digested with EcoRI and cloned into pPDM His which had been digested with Eco72I and EcoRI. The sequence was confirmed through sequence analysis and then transformed into BLR pLys S and BLR which is co-transformed with CODONPLUS® ~~CodonPlus~~ RP.

Please replace the paragraph beginning at page 110, line 18, with the following redlined paragraph:

The PCR product was digested with EcoRI and cloned into pPDM His which had been digested with Eco72I and EcoRI. The sequence was confirmed and then transformed into BLR pLys S and BLR which is co-transformed with CODONPLUS® ~~CodonPlus~~ RP.

Please replace the table beginning at page 111, line 20, with the following redlined table:

Table L

Experimental Design of WT1 Immunization in Mice

Histology Group	Corixa Group	Treatment Description	Dose Level	Total No. (Females)
1	0	No treatment	0	4
2	1.1	MPL®-SE (adjuvants alone), 6x, 1 week apart	10ug	4
3	1.2	MPL®-SE, 3x, 2 weeks apart	10ug	4
4	2.1	Ra12-WT1+ MPL®-SE, 6x	25ug	4
5	2.2	Ra12-WT1 + MPL®-SE, 3x	25ug	4
6	3.1	Ra12-WT1 + MPL®-SE, 6x	100ug	4
7	3.2	Ra12-WT1 + MPL®-SE, 3x	100ug	4
8	4.1	Ra12-WT1 + MPL®-SE, 6x	1000ug	4
9	4.2	Ra12-WT1 + MPL®-SE, 3x	1000ug	4

Please replace the paragraph beginning at page 112, line 2, with the following redlined paragraph:

Vaccination to WT1 protein using MPL®-SE as adjuvant, in a multiple dose titration study (doses ranging from 25µg, 100µg to 1000µg WT1 protein) in female C57/B6 mice elicited a strong WT1-specific antibody response (Figure 19) and cellular T-cell responses (Figure 20).

Please replace the paragraph beginning at page 120, line 3, with the following redlined paragraph:

Recombinant Ra12-WT1 concentration: 0.5 – 1.0 mg/ml; Buffer: 10-20 mM Ethanolamine, pH 10.0; 1.0 – 5.0 mM Cysteine; 0.05 % ~~Tween~~TWEEN®-80 (Polysorbate-80); Sugar: 10% Trehalose (T5251, Sigma, MO) 10% Maltose (M9171, Sigma, MO) 10% Sucrose (S7903, Sigma, MO) 10% Fructose (F2543, Sigma, MO) 10% Glucose (G7528, Sigma, MO).

Please replace the paragraph beginning at page 120, line 16, with the following redlined paragraph:

According to this example, WT1 protein in combination with MPL®-SE induces a strong Ab and Interferon-γ (IFN-γ) response to WT1. Described in detail below are the methods used to induce WT1 specific immune responses following WT1 protein immunization using MPL®-SE or ~~Enhanzyn~~ENHANZYN® as adjuvant in C57/B6 mice.

Please replace the paragraph beginning at page 120, line 20, with the following redlined paragraph:

C57BL/6 mice were immunized with 20 µg rRa12-WT1 combined with either MPL®-SE or ENHANZYN®~~Enhanzyn~~ adjuvants. One group of control mice was immunized with rRa12-WT1 without adjuvant and one group was immunized with saline alone. Three intramuscular (IM) immunizations were given, three weeks apart. Spleens and sera were harvested 2 weeks post-final immunization. Sera were analyzed for antibody responses by ELISA on plates coated with Ra12-WT1 fusion, Ra12 or WT1TRX. Similar levels of IgG2a and IgG1 antibody titers were observed in mice immunized with Ra12-WT1+MPL®-SE and Ra12-WT1+~~Enhanzyn~~ENHANZYN®. Mice immunized with rRa12-WT1 without adjuvant showed lower levels of IgG2a antibodies.

Please replace the paragraph beginning at page 121, line 1, with the following redlined paragraph:

CD4 responses were assessed by measuring Interferon-γ production following stimulation of splenocytes *in vitro* with rRa12-WT1, rRa12 or with WT1 peptides p6, p117 and p287. Both adjuvants improved the CD4 responses over mice immunized with rRA12-WT1 alone. Additionally, the results indicate that rRA12-WT1+MPL®-SE induced a stronger CD4 response than did rRA12-WT1+~~Enhanzyn~~ENHANZYN®. IFN-γ OD readings ranged from 1.4-1.6 in the mice immunized with rRA12-WT1+MPL®-SE as compared to 1-1.2 in the mice immunized with rRA12-WT1+~~Enhanzyn~~ENHANZYN®. Peptide responses were only observed against p117, and then only in mice immunized with rRa12-WT1+MPL®-SE. Strong IFN-γ responses to the positive control, ConA, were observed in all mice. Only responses to ConA were observed in the negative control mice immunized with saline indicating that the responses were specific to rRA12-WT1.

Please replace the paragraph beginning at page 130, line 19, with the following redlined paragraph:

Total mRNA from 2 x 10^6 cells from a WT1 specific CD8+ T cell clone is isolated using ~~Trizol~~ TRIZOL® reagent and cDNA is synthesized using ~~Ready-to-go~~READY-TO-GO® kits (Pharmacia). To determine Vα and Vβ sequences in a clone, a panel of Vα and Vβ subtype specific primers are synthesized (based on primer sequences generated by Clontech, Palo Alto, CA) and used in RT-PCR reactions with cDNA generated from each clone. The RT-PCR reactions demonstrate which Vβ and Vα sequence is expressed by each clone.